In the United States Court of Federal Claims

No. 11-693V
(Filed: May 23, 2018)[1]

OLIVIA BENDER, **Petitioner,** **v.** **SECRETARY OF HEALTH AND HUMAN SERVICES,** **Respondent.**	**National Childhood Injury Vaccination Act, 42 U.S.C. §§ 300aa-1 et seq.; Causation in Fact; Hepatitis A Vaccine; Meningococcal Vaccine; Menactra; Transverse Myelitis; Expert Testimony; Molecular Mimicry; Epidemiological Studies; Remand.**

Bruce W. Slane, The Law Office of Bruce W. Slane, P.C., 188 East Post Road, Suite 205, White Plains, NY 10601, for Petitioner.

Chad A. Readler, C. Salvatore D'Alessio, Catharine E. Reeves, Alexis B. Babcock, Lara A. Englund, United States Department of Justice, Civil Division, Torts Branch, P.O. Box 146, Benjamin Franklin Station, Washington, D.C. 20044, for Respondent.

OPINION AND REMAND ORDER

WILLIAMS, Judge.

In the underlying action before the Special Master, Petitioner claimed that she developed transverse myelitis ("TM") as a result of receiving the meningococcal and Hepatitis A vaccines, and sought compensation under the National Vaccine Injury Compensation Program. The Special Master denied compensation, finding that Petitioner failed to establish that her vaccinations caused her TM, and Petitioner timely filed this Petition for Review.

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[1] Pursuant to Vaccine Rule 18 of the Rules of the United States Court of Federal Claims, the Court issued its opinion under seal to provide the parties an opportunity to submit redactions. The parties did not propose any redactions. Accordingly, the Court publishes this opinion.

Petitioner argues that in analyzing Althen prong one[2] the Special Master misconstrued and mischaracterized the testimony of Petitioner's expert immunologist, Dr. Vera Byers. In particular, Petitioner contends that the Special Master erroneously concluded that Dr. Byers conceded that molecular mimicry was inapplicable as a mechanism that could cause TM. As Petitioner points out, Dr. Byers did exclude molecular mimicry in a limited sense as a plausible biological mechanism, but not in the broad-based manner the Special Master found. While Dr. Byers' testimony was not a model of clarity, her testimony did, as Petitioner argues, reject "widespread" molecular mimicry as a causal mechanism, while at the same time embracing individualized molecular mimicry as a causal mechanism. Dr. Byers expressly relied upon individualized molecular mimicry as a plausible biological mechanism which could cause autoimmune diseases and TM as a result of vaccines. Because the Special Master misconstrued Dr. Byers' testimony, this matter is remanded for a reevaluation of her testimony and a re-analysis of the three Althen factors based on that reevaluation.[3]

Factual Background

On May 29, 2009, Petitioner received the Hepatitis A and meningococcal (marketed as "Menactra") vaccines after a physical examination. Petitioner was 14 years old and had no prior health problems, nor any adverse reactions to her first Hepatitis A vaccination received on May 10, 2001. While on a teen camping trip in Arizona on July 9, 2009, 41 days following the vaccinations, Petitioner suffered a sudden onset of middle and lower back pain. The next day, while on a bus, Petitioner suffered a sudden onset of numbness, tingling and paresthesia from the waist down, resulting in her inability to use her legs and causing her to collapse on the ground shortly after walking off the bus. Petitioner was immediately taken to the nearest hospital, Kingman Regional Medical Center in Kingman, Arizona, where a variety of tests and lab work were performed, including CT scans of Petitioner's cervical, thoracic and lumbar spine; a urinalysis; and a complete blood count. On examination, Petitioner had no sensation below her umbilicus and no reflexes in her lower extremities.

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[2] In Althen v. Secretary of Health & Human Services, the Federal Circuit set forth a three-pronged test for proving causation in vaccine cases: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury. 418 F.3d 1274, 1278 (Fed. Cir. 2005).

[3] Petitioner also claims that the Special Master raised Petitioner's burden of proof by improperly requiring specific medical literature under Althen prong one and test results under Althen prong two. It is not clear to what extent these considerations impacted the Special Master's decision. Nonetheless, because the Special Master's misconstruction of Dr. Byers' testimony permeated his causation analysis, the Court vacates the Special Master's decision and directs him to reevaluate causation. As such, the Special Master shall reevaluate the evidence -- including the medical literature and records such as test results -- based upon his reconsideration of Dr. Byers' testimony. On remand, the Special Master shall clearly articulate how the medical literature and absence of test results informed his decision.

Petitioner was transferred to Sunrise Hospital in Las Vegas, Nevada for a neurological consult. The transfer admission record notes the most likely diagnosis was TM. Sunrise performed MRIs on July 10 and 14, 2009. The MRI of Petitioner's thoracic spine taken on July 10th revealed "abnormal T2 signal and abnormal enhancement within the gray matter [of] the cord at the T11-T12 levels" which "findings may represent an acute transverse myelitis." Pet'r's Ex. 15, at 146.

A repeat MRI of Petitioner's thoracic spine taken on July 14, 2009, revealed an "abnormal signal in the spinal cord from T8 through T12 compatible with a clinical history of transverse myelitis." A repeat MRI of her lumbar spine also revealed "abnormal increased signal in the distal spinal cord compatible with transverse myelitis." A mycoplasma IgM serology also taken on July 14, 2009, indicated that no mycoplasma pneumoniae antibodies were detected. Although the test response was negative, the report mistakenly listed the IgM interpretation under the positive column. A mycoplasma pneumoniae PCR analysis was also negative. Petitioner's doctors initially relied upon the false IgM reading, diagnosing her with TM secondary to a mycoplasma infection and treating her with a course of azithromycin.

On July 21, 2009, Petitioner was transferred via air ambulance to Blythedale Children's Hospital in Valhalla, New York, for inpatient rehabilitation closer to home. There, Petitioner began physical and occupational therapy focused on regaining mobility and sensation in her lower extremities, and training on management of her own care. Petitioner was discharged from Blythedale on September 4, 2009, and on November 6, 2009, underwent additional spinal MRIs which showed T2 signal intensity changes in the spinal cord from T5 to T8-9.

Petitioner has continued treatment at Kennedy Kreiger's International Center for Spinal Cord Injury. Despite rigorous rehabilitative therapies, to date Petitioner has not regained motor or sensory functions in her lower extremities. While none of Petitioner's treating physicians have associated her TM with the vaccinations she received seven weeks prior to the onset of her symptoms, there is no evidence that they were aware that the mycoplasma infection test result in her patient records was mistaken. At the time Petitioner was seen by the treating physicians, Petitioner's mycoplasma IgM serology mistakenly indicated a positive IgM interpretation identified by the laboratory. In Dr. Byers' view, these doctors did not implicate Petitioner's vaccinations as a cause of the TM because "they already thought they had an answer." Tr. 366.

On October 19, 2011, Petitioner filed a timely petition under the National Childhood Vaccine Injury Act, 42 U.S.C. §300aa-10, et seq., alleging that she suffered TM as a result of receiving the Meningococcal and Hepatitis A vaccines. The parties filed numerous expert reports and substantial medical literature. On February 9-10, 2017, the Special Master conducted an entitlement hearing, and on October 6, 2017, issued his decision denying entitlement. On November 3, 2017, Petitioner filed a Motion for Review requesting that the Court set aside the decision and rule in the Petitioner's favor, or in the alternative, remand the case to the Special Master for further consideration.

Discussion

Jurisdiction and Standard of Review

In Vaccine Act cases, the Court of Federal Claims has "jurisdiction to undertake a review of the record of the proceedings" and may: (1) uphold the findings of fact and conclusions of law and sustain the special master's decision; (2) set aside any of the findings of fact or conclusions of law "found to be arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law and issue its own findings of fact and conclusions of law" or (3) "remand the petition to the special master for further action in accordance with the court's direction." 42 U.S.C. § 300aa-12(e)(2)(A)-(C) (2012); Doe 93 v. Sec'y of Health & Human Servs., 98 Fed. Cl. 553, 564-65 (2011).

"Findings of fact of the special master are reviewed under the arbitrary and capricious standard, conclusions of law are reviewed under the not in accordance with law standard, and discretionary rulings are reviewed under the abuse of discretion standard." Broekelschen v. Sec'y of Health & Human Servs., 89 Fed. Cl. 336, 343 (2009), aff'd, 618 F.3d 1339 (Fed. Cir. 2010) (internal citations and quotation marks omitted). The Court's role is not to "reweigh the factual evidence," "assess whether the special master correctly evaluated the evidence," or "examine the probative value of the evidence or the credibility of the witnesses." Lampe v. Sec'y of Health & Human Servs., 219 F.3d 1357, 1360 (Fed. Cir. 2000) (internal citation and quotation marks omitted). However, the Court has "a duty to ensure that the special master has properly applied Vaccine Act evidentiary standards, 'considered the relevant evidence of record, drawn plausible inferences and articulated a rational basis for [his] decision.'" Paluck v. Sec'y of Health & Human Servs., 786 F.3d 1373, 1380 (Fed. Cir. 2015) (quoting Hines ex rel. Sevier v. Sec'y of Dep't of Health & Human Servs., 940 F.2d 1518, 1528 (Fed. Cir. 1991)) (alteration in original).

Burden of Proof under the Vaccine Act

In the seminal case of Althen v. Secretary of Health & Human Services, the Federal Circuit articulated the petitioner's burden to demonstrate causation-in-fact as follows:

> [Petitioner's] burden is to show by preponderant evidence that the vaccination brought about her injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury.

418 F.3d 1274, 1278 (Fed. Cir. 2005).

Petitioner must prove causation-in-fact "by a preponderance of the evidence." 42 U.S.C. § 300aa-13(a)(1)(A). The Federal Circuit "has interpreted the preponderance of the evidence standard referred to in the Vaccine Act as one of proof by a simple preponderance, of more probable than not causation." Althen, 418 F.3d at 1279 (internal citation and quotation marks omitted). Petitioner's claim must be "substantiated by medical records or medical opinion . . . ." Id (emphasis in original). "It is not plaintiff's burden to disprove every possible ground of

causation suggested by defendant nor must the findings of the Court meet the standards of the laboratorian." Bunting v. Sec'y of Dep't of Health & Human Servs., 931 F.2d 867, 873 (Fed. Cir. 1991) (internal citation and quotation marks omitted).

The Federal Circuit "adopt[ed] the Restatement rule for purposes of determining vaccine injury, that an action is the legal cause of harm if that action is a substantial factor in bringing about the harm, and that the harm would not have occurred but for the action." Shyface v. Sec'y of Health & Human Servs., 165 F.3d 1344, 1352 (Fed. Cir. 1999) (internal citation and quotation marks omitted).

To effectuate Congress's intent and advance the objectives of the Vaccine Act, causation is determined on a case-by-case basis, as follows:

> Causation in fact under the Vaccine Act is thus based on the circumstances of the particular case, having no hard and fast per se scientific or medical rules. The determination of causation in fact under the Vaccine Act involves ascertaining whether a sequence of cause and effect is "logical" and legally probable, not medically or scientifically certain. Thus, for example, causation can be found in vaccine cases based on epidemiological evidence and the clinical picture regarding the particular child without detailed medical and scientific exposition on the biological mechanisms.
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> Furthermore, to require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program. The Vaccine Act does not contemplate full blown tort litigation in the Court of Federal Claims. The Vaccine Act established a federal "compensation program" under which awards are to be "made to vaccine-injured persons quickly, easily, and with certainty and generosity." The program is supposed to be "fair, simple, and easy to administer."

Knudsen v. Sec'y of Dep't of Health & Human Servs., 35 F.3d 543, 548-49 (Fed. Cir. 1994) (internal citations omitted).

The Vaccine Act permits proof of causation through "the use of circumstantial evidence envisioned by the preponderance standard." Capizzano v. Sec'y of Health & Human Servs., 440 F.3d 1317, 1325 (Fed. Cir. 2006) (internal citation and quotation marks omitted). As the Federal Circuit has consistently reiterated, under the Vaccine Act, "close calls regarding causation are resolved in favor of injured claimants." Althen, 418 F.3d at 1280.

If the petitioner provides preponderant evidence that the vaccine caused petitioner's injury under the Althen test, the burden then shifts to the Secretary of the Department of Health and Human Services to prove, by a preponderance of the evidence, that a factor unrelated to the vaccination actually caused the injury. 42 U.S.C. § 300aa-13(a)(1)(B). If the Secretary fails to meet this burden, the petitioner is entitled to compensation. de Bazan v. Sec'y of Health & Human Servs., 539 F.3d 1347, 1352 (Fed. Cir. 2008). "So long as the petitioner has satisfied all three

prongs of the Althen test, she bears no burden to rule out possible alternative causes." Id. (internal footnote and citation omitted).

The Special Master's Decision Denying Entitlement

The Special Master found that "[w]hile Petitioner makes a number of persuasive points rebutting Respondent's proposed alternative explanations for her illness" there was "insufficient reliable evidence to support the conclusion that the two vaccines she received are themselves reasonable explanations for it." Bender v. Sec'y of Health & Human Servs., No. 11-693V, 2017 WL 5381628, at *19 (Fed. Cl. Spec. Mstr. Oct. 6, 2017) (emphasis in original).

Althen Prong One

Under Althen prong one, the Special Master found that while Petitioner's general theory, that a vaccine could cause a demyelinating condition, was consistent with other successful causation theories frequently proposed in Program cases, Petitioner's immunologic expert Dr. Byers "conceded at the outset that the mechanism most frequently offered by Program petitioners to explain how a vaccine might precipitate an autoimmune condition like TM – molecular mimicry[4] – is inapplicable in this case." Id. Due to what the Special Master characterized as Dr. Byers' "concession," the Special Master found that Petitioner had failed to establish that the vaccines Petitioner received could cause TM.

The Special Master ruled that the most reliable scientific and medical evidence supports the conclusion that if Petitioner's alternative mechanisms, bystander activation or epitope spreading, were to play any contributory role in the pathogenesis of an autoimmune condition like TM, molecular mimicry had to be implicated. Specifically, the Special Master determined that for bystander activation or epitope spreading to occur, "there must first be an autoimmune response to a specific antigen presented by a vaccine component that tricks the immune system into that response – in other words, via the mechanism of molecular mimicry. . ." Id. at *20 (emphasis omitted). The Special Master determined that Dr. Byers "virtually admitted that either of her proposed mechanisms presupposes molecular mimicry having occurred first." From this, the Special Master found that Dr. Byers' concession that molecular mimicry was inapplicable significantly harmed Petitioner's overall causation theory. Id.

The Special Master rejected Petitioner's theory that the immunologic simulation that all vaccinations generally provide could result in an autoimmune demyelinating condition like TM. The Special Master determined that Petitioner had not offered any evidence connecting vaccines to TM other than merely through their recognized pro-inflammatory capacities, as opposed to cross-reactivity caused by a vaccine component, which the Special Master found Dr. Byers to have disavowed by virtue of her "concession" that molecular mimicry was not implicated here.

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[4] Molecular mimicry refers to a similarity between the protein structure of a vaccine antigen and a protein in the human body. The theory is that this similarity enables immune cells that respond to the vaccine antigen to also "cross-react" with the human protein, thereby triggering an autoimmune attack against the protein.

The Special Master gave "some weight" to an epidemiologic study offered by Respondent which suggested no association between the vaccines at issue in this case and TM. Id. at *21. The Special Master found that Respondent's study, Acute Demyelinating Events Following Vaccines: A Case-Centered Analysis by R. Baxter, et al., was a "very recent, scientifically-reliable retrospective case-centered" one, which suggested that there is no statistically significant association between Menactra and/or Hep A and TM. Id. The Special Master found "the existence of such [epidemiological] evidence only undercuts the conclusion that the relevant vaccines could have caused Petitioner's TM." Id.

The Special Master found that Petitioner's theory of causation "relie[d] too heavily on points general to the association between certain vaccines and autoimmune illness (more often than not mediated by the inapplicable mechanism of molecular mimicry), without offering more reliable and persuasive evidence that the vaccines Ms. Bender actually received can cause the specific autoimmune disease she experienced." Id. (emphasis in original).

The Special Master concluded:

> [Petitioner] has offered nothing in the form of reliable scientific or medical evidence that addresses the specific pathogenicity of the two vaccines in dispute, nor anything connecting other vaccines to TM based merely on their recognized pro-inflammatory capacities (as opposed to a cross reactivity caused by a vaccine component – something Dr. Byers disavows occurred here). And the literature she relies upon does not reliably establish that cytokines can instigate an autoimmune process – as opposed to amplify an ongoing autoimmune condition.

Id. at *20 (emphasis in original).

Althen Prong Two

The Special Master found that Petitioner failed to meet the second, "did cause" Althen prong because "evidence of the development of a disease temporally following a vaccination is insufficient on its own to establish causation." Id. at *22 (citing Grant v. Sec'y of Dep't Health & Human Servs., 956 F.2d 1144, 1148 (Fed. Cir. 1992). The Special Master acknowledged that the evidentiary record largely supported Petitioner's challenge to Respondent's proposed alternative explanations for her TM. The Special Master recognized that Petitioner "successfully established that the IgM levels relied upon by initial treaters as pointing to a mycoplasma infection as the cause of her TM were a false positive" and that "the record contains no other clues as to other alternative causes for her condition." Id. Nonetheless, the Special Master found that merely identifying the vaccine as causal because of its existence as a "known, pre-onset occurrence [was] insufficient to establish causation without corroborative record proof demonstrating the 'logical sequence of cause and effect' required." Id. (citing Grant, 956 F.2d at 1148).

The Special Master noted that his Althen prong two analysis relied in part on his finding that Petitioner had failed to carry her burden of proof with respect to prong one, explaining that "[i]n a case where a claimant successfully met that initial burden by establishing a reliable association between the vaccine and the alleged injury, the lack of a persuasive alternative

explanation for a particular petitioner's illness following vaccination would be far more compelling." Id. at *22, n 34.

Althen Prong Three

The Special Master found that Petitioner's evidence supporting the medical acceptability of the 42-day period between vaccination and the onset of Petitioner's TM came largely from Dr. Byers who relied on an article reflecting some wide time intervals between the onset of TM and several vaccines. See N. Agmon-Levin, et al., Transverse Myelitis and Vaccines: A Multi-Analusis, Lupus 18:1198-1204 (2009) ("Agmon-Levin"). The Special Master however, credited Dr. Forsthuber's testimony, Respondent's expert immunologist, that Agmon-Levin was based on individual case reports that "lacked sufficient medical reliability to offer reliable timeframes applicable to Ms. Bender's claim." Bender 2017 WL 5381628, at *23. Where TM is the relevant injury, the Special Master found "the disparate nature of the case studies Agmon-Levin draws from makes it impossible to deem its timeframe conclusions reliable." Id. The Special Master found that Petitioner offered no other literature establishing that any vaccine could initiate the upregulation of cytokines for a six-week period sufficient in severity and degree to cause a sudden autoimmune condition like TM.

The Special Master rejected Petitioner's expert Dr. Chen's conclusion that the state of Petitioner's lesions suggested that the autoimmune process was under way prior to the 42-day post vaccination onset of her TM. The Special Master found that Petitioner did not otherwise offer evidence supporting Dr. Chen's opinion that TM would be characterized by a subclinical onset that would predate obvious symptoms.

While the Special Master did acknowledge that 42 days has been deemed acceptable with respect to the timeframe for other vaccines to establish a response like TM, he noted that such a timeframe was more applicable to cases involving the mechanism of molecular mimicry, which the Special Master had determined Petitioner's immunologist conceded was inapplicable. Because the Special Master found Petitioner had not credibly established that the vaccines could cause TM via any proposed mechanism under Althen prong one, the Special Master found she had not established that the autoimmune process which resulted in her TM would take as long as it did. The Special Master concluded that Petitioner did not establish that the vaccines could cause TM in 42 days.

Petitioner's Objections

Petitioner alleges that the Special Master misconstrued and mischaracterized Dr. Byers' testimony and medical theories. Specifically, Petitioner takes issue with the Special Master's conclusion that Dr. Byers "conceded at the outset that the mechanism most frequently offered by Program petitioners to explain how a vaccine might precipitate an autoimmune condition like TM – molecular mimicry – is inapplicable in this case." Id. at *19. Petitioner contends that the Special Master's determination was contrary to Dr. Byers' report and testimony, and that Dr. Byers actually testified that there were two types of molecular mimicry, one that is widespread and one that occurs on an individual basis. Petitioner argues that the Special Master's misconstruction and

mischaracterization of this critical testimony was carried through his entire analysis and ultimately led to his improper conclusion that Petitioner had not carried out her burden of proof.

The Special Master did determine that Dr. Byers "conceded" molecular mimicry was inapplicable in this case, stating:

> At the outset, Dr. Byers made a significant concession relevant to her theory. She unequivocally agreed that molecular mimicry was not a plausible biologic mechanism at work herein, admitting that she could not identify sufficient homology between antigens from components of the vaccines Ms. Bender received and self-protein structures. Byers Rep. at 7; Tr. at 47 ("I excluded molecular mimicry, because there is no evidence that there is molecular mimicry between the two vaccines and the association with autoimmune reactions").

Id. at *5 (emphasis in original) (internal footnote omitted).

On direct examination, Dr. Byers testified:

A. I think the main four causes that people look at for vaccines, apart from there's – it's molecular mimicry, and I excluded molecular mimicry because there is no evidence that there is molecular mimicry between the two vaccines and the association with autoimmune reactions. There is a molecular mimicry with the . . . meningococcus group B, but that's not included in the vaccine. Go ahead?

Q. What is molecular mimicry?

A. Molecular mimicry is extremely simple, and everybody loves it, because it's so simple. It simply means that the 3D structure of the antigen that is presented on the surface of the macrophage generates an immune response which cross-reacts with some of the body's own components and therefore it triggers an autoimmune reaction.

Q. Okay, and you came to a conclusion as to the mechanism which caused Ms. Bender's transverse myelitis. Is that correct?

A. I excluded molecular mimicry -- I can't completely exclude molecular mimicry, because we don't really understand the specificity of the T cells; however, I did conclude that I could not support that in the literature.

Tr. 47-48.

However, later in her direct examination, Dr. Byers testified that molecular mimicry could have been a mechanism for Petitioner's TM, stating:

Q. Well, if you can -- in relation to Ms. Bender's May 29th, 2009 vaccinations, is it your opinion that bystander activation was a -- the mechanism of her transverse myelitis?

A. It's either that, in which case -- in which I think Dr. Lotze agrees with me, or alternatively, it could be molecular mimicry.

Q. And when you say alternatively it could be molecular mimicry, how -- can you explain that?

A. Yes. Molecular mimicry refers to the fact that generally when an antigen is presented to the immune system, of the wide variety of specificities, there are a few cells that are just exquisitely directed towards killing the darn thing. And they immediately swarm in and start to destroy the antigen.

However, in a few cases, and this depends upon the genetics of the person, the individual genetics, as well as the way in which the antigen just happened to be digested in the macrophage and presented on the surface. For some -- in that case, there might not be one -- some of those very, very specific cells that can immediately zoom in there to the area, and so therefore you wind up with kind of a crowded -- sorry -- you wind up with kind of a push and shove situation where a bunch of different lymphocytes, primarily T cells, that are not -- that do not have the specificity so that they can compete like they normally do, and so then the -- the specificity of the T cells involves -- begins to spread, and it includes those autoreactive cells that have been stimulated, and so then can go after.

So it's basically still molecular mimicry, but it's molecular mimicry on an individual basis.

Q. And that would be different than the molecular mimicry that you initially mentioned?

A. It would be different because the initial molecular mimicry is so widespread in the population, that you will be able to see it. Like, for example, with swine flu and Guillain-Barre, whereas in this case, it's so individual and so rare that you actually can't prove it in humans, you have to go into animals.

Id. at 50-51 (emphasis added).

Dr. Byers opined that bystander activation was another mechanism that explains that Petitioner's vaccines could cause TM and reiterated "molecular mimicry on an individual basis" as a "reputable medical explanation" of the cause of Petitioner's TM, testifying:

Q. What is polyclonal activation?

A. Polyclonal activation would also be called bystander activation. Polyclonal activation is when you have cytokines that are released by either an infection or a vaccination which not only activates these antigen-specific immune system, but also activates other reactive cells as well, so they are then activated and can go after their true target, which is actually autologous self-antigens.

Q. And bystander activation, in your opinion, is a reputable medical explanation of the cause of Ms. Bender's transverse myelitis?

A. Oh, yes, one of them. There's about six of -- six different very, very well-established causes, and I have eliminated all except two.

Q. And the two would be bystander activation and epitope spreading, or -- and/or molecular mimicry on an individual basis?

A. That's right.

Id. at 53-54.

The theory of bystander activation holds that cytokines triggered by a vaccination can "activate" immune cells that are specific for self-antigens, thus causing an autoimmune attack against those self-antigens. Respondent's expert in immunology, Dr. Forsthuber, explained that a vaccine cannot "activate" a self-antigen unless there is a sufficient similarity between the vaccine antigen and the self-antigen to allow cross-reaction, which again requires molecular mimicry.

The Special Master himself found that Dr. Byers recognized that molecular mimicry was at play in another potential vaccine-related mechanism for Petitioner's TM,"epitope spreading." Epitope spreading occurs when "in an inflammatory state, there is strong local activation of antigen-presenting cells. Such activation may result in overprocessing and overpresentation of antigens, thus priming large numbers of T cells with broad specificities, possibly against self antigens." Pet'r's Ex. 30 Tab 2, at 641. Dr. Byers testified that epitope spreading is analogous to molecular mimicry, as it is dependent on the genetics of the individual to engage the less specific T or B cells that are more specific for the "self" antigens than actually for the vaccine antigens. Dr. Forsthuber also determined that Dr. Byers had opined that molecular mimicry was a causal mechanism, stating that Dr. Byers' testimony regarding epitope spreading encompassed a scenario more along the lines of molecular mimicry, testifying "I think she was really more referring to molecular mimicry." Tr. 303. The Special Master acknowledged this aspect of Dr. Byers' testimony on molecular mimicry, stating: "Dr. Byers characterized epitope spreading as a kind of molecular mimicry unique to susceptible individuals who cannot muster a proper focused immunologic response to vaccine antigens, resulting in an autoimmune attack instead. Tr. at 52 ("it's just molecular mimicry on a very individual basis"), 53, 60-61 ("in the case of epitope spreading, those highly specific cells that could very rapidly eliminate the infection could not be there, primarily on a genetic basis")". Bender, 2017 WL 5381628, at *6.

Despite testimony in which Dr. Byers expressly relied upon molecular mimicry as a plausible mechanism for Petitioner's TM, the Special Master concluded that Dr. Byers broadly excluded molecular mimicry from involvement in Petitioner's TM, stating "[i]n Dr. Byers's view, several immune mechanisms other than direct molecular mimicry could have been involved in the pathogenesis of Ms. Bender's TM." Id. (emphasis added). Because the Special Master failed to take into account Dr. Byers' testimony that molecular mimicry on an individual basis was implicated here, he erroneously concluded that Dr. Byers had completely disavowed molecular mimicry as a mechanism at play in vaccine causation of Petitioner's TM. This caused the Special Master to discredit Dr. Byers' proposed mechanisms of epitope spreading and bystander activation because they required molecular mimicry - - a mechanism he believed Dr. Byers had rejected.

Given Dr. Byers' distinction between two types of molecular mimicry - - generalized "widespread molecular mimicry" and individualized molecular mimicry, this Court finds that Dr. Byers did not make the broad concession about the inapplicability of molecular mimicry that the Special Master attributed to her. The Special Master's misconstruction of Petitioner's expert's testimony may have impacted his legal conclusion that Petitioner failed to establish that the meningococcal and Hepatitis A vaccines can cause TM. See Raymo v. Sec'y of Health & Human Servs., No. 11-0654V, 2014 WL 1092274, at *21 (Fed. Cl. Spec. Mstr. Feb. 24, 2014) (concluding "there is adequate evidence that vaccinations in general can cause ATM. Although the precise biological mechanism has not been determined, molecular mimicry and bystander activation theories are biologically probable"). As such, this matter is remanded to the Special Master for a reevaluation of Dr. Byers' testimony and the Althen factors.

Petitioner also argues that the Special Master raised Petitioner's burden of proof by requiring specific medical research under Althen prong one, and test results under Althen prong two. Because the Special Master's conclusions about both the medical literature and test results were informed by his analysis of the expert testimony - - including that of Dr. Byers - - the Special Master shall on remand assess the literature and absence of test results in light of his reevaluation of Dr. Byers' testimony.

Finally, Petitioner argues that the Special Master's conclusion that she failed to show a temporal relation between the vaccinations and her injury was arbitrary and capricious. Petitioner contends that her burden is to present "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." Pet'r's Mot. 14 (internal citation and quotation marks omitted). Petitioner contends that the onset of TM in this case, 42 days following the vaccinations, is considered an acceptable timeframe by this Court and the scientific community for vaccine mediated autoimmune disease. See Crosby v. Sec'y of Dep't of Health & Human Servs., No. 08-799V, 2012 WL 3758430, at *4 (Fed. Cl. Spec. Mstr. June 20, 2012) (recognizing that vaccine-mediated autoimmune disease, including TM, can take up to 42 days to surface).

The Special Master's conclusion that Petitioner failed to establish the requisite temporal connection between Petitioner's vaccines and TM was largely dependent upon his conclusion that Dr. Byers excluded molecular mimicry as a mechanism that could cause TM. The Special Master stated: "[a]dmittedly, 42 days has been deemed reasonably acceptable with respect to the timeframe for other vaccines to establish an autoimmune response like TM. But such a timeframe is more applicable to cases involving the mechanism of molecular mimicry – something Petitioner's own immunologist agrees was inapplicable." Bender, 2017 WL 5381628, at *23 (emphasis and internal citation omitted). As a result, the Special Master found that because "Petitioner could not credibly establish that the vaccines she received could cause TM via any of the proposed mechanisms, she has also not established that the autoimmune process resulting in the disease would take as long as it purportedly did." Id.

Because the Special Master based his Althen prong three analysis on his misconstruction of Dr. Byers' testimony i.e. that Dr. Byers had stated that molecular mimicry was inapplicable in this case, he shall, on remand, reevaluate Dr. Byers' testimony and the temporal relationship between Petitioner's vaccines and her TM.

Conclusion

The decision of the Special Master is vacated, and this matter is remanded to the Special Master for a reevaluation of Dr. Byers' testimony and a reanalysis of the three Althen factors based on that reevaluation.

1. On remand, the Special Master shall reevaluate the opinion of Dr. Byers, considering the entirety of her testimony and her distinction between widespread and individualized molecular mimicry.

2. Because the Special Master's interpretation of Dr. Byers' testimony affected his entire causation analysis, the Special Master shall reevaluate the evidence -- including the medical literature and records, such as test results -- based upon his reconsideration of Dr. Byers' testimony.

Pursuant to 42 U.S.C. § 300aa-12(e)(2), the Court allows 90 days for the completion of proceedings on remand.

s/Mary Ellen Coster Williams
MARY ELLEN COSTER WILLIAMS
Judge